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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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HAYNES AND BOONE, LLP
901 MAIN STREET, SUITE 3100
DALLAS, TX 75202

EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/092,769	KHOSRAVI ET AL.	
	Examiner	Art Unit	
	Brandon J Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-55* is/are pending in the application.

4a) Of the above claim(s) *17-24,31-39 and 41-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-30 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

The Election filed on November 15, 2004 in response to the Restriction Requirement of August 10, 2004 is acknowledged and has been entered. Applicants have elected Group II, Claims 25-31, and further elected IGF-1 as the growth factor from those listed in Claim 26, IGFBP-3 from those listed in Claim 27, and PSA as the tumor marker from those listed in claim 29.

Applicant's election with traverse of Group II, Claims 25-31 is acknowledged. The traversal is on the ground(s) that a search of the prior art relevant to claims 25-31 would necessarily reveal any prior art relevant to the subject matter of Claim 40 in Group VII. Specifically, Applicants submit that such prior art related to a method for discriminating between benign disorders and cancer would necessarily reveal any prior art related to a method for discriminating between benign prostate disorders and prostate cancer, because the method of claims 25-31 cannot be practiced without practicing the method of claim 40. Therefore, Applicants assert that a search of the prior art relevant to the claims of Group II would impose no more of a burden on the Examiner than a search of the prior art relevant to the Claims of Group VII. These arguments have been considered and are found persuasive. Group VII, Claim 40, will be rejoined with Group II, claims 25-31 for consideration on the merits.

For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 17-55 are currently pending in the application.

Claims 17-24, 31-39 and 41-55 are withdrawn from consideration as being drawn to a non-elected invention.

Claims 25-30 and 40 are currently under consideration.

Information Disclosure Statement

The Information Disclosure Statement filed on May 6, 2002 is acknowledged and considered. A signed copy of the IDS is attached hereto.

Application Data Sheet/Specification

The Application Data Sheet/Specification is objected to because of the following informalities: The Domestic Priority Information needs to be updated to properly identify that this application is a Continuation of 09/484,903 filed on 01/18/2000, now U.S. Patent 6,448,086.

Appropriate correction is required.

Claim Objections

Claims 26, 27 and 29 are objected to because of the following informalities: Claims 26, 27 and 29 are drawn to non-elected inventions. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for discriminating between benign prostate disorders and prostate cancer by calculating a ratio based on at least two of the measured concentrations of either IGF-I, IGFBP-3, and PSA does not reasonably provide enablement for providing a means for discriminating between any and/or all benign disorders and cancers by calculating a ratio based on at least two of the measured concentrations of either IGF-I, IGFBP-3, and PSA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The instant claims read on a diagnostic method comprising: (i) collecting a body fluid from an individual; (ii) measuring an insulin-like growth factor binding protein (IGFBP) concentration; (iii) measuring a growth factor concentration; (iv) measuring a tumor marker concentration; and (v) calculating an indicator ratio based upon at least two of the measured concentration, wherein the indicator ratio provides a means for discriminating between benign disorders and cancer. The claims are further drawn to wherein the growth factor is IGF-I (claim 26), the IGFBP is IGFBP-3 either total or intact (claim 27-28), and the tumor marker is PSA (claim 28).

Therefore, the claims read on providing a means for discriminating between any and/or all benign disorders and cancers by calculating a ratio based on at least two of the measured concentrations of IGF-I, IGFBP-3 or PSA. Thus, it appears that at least two of the "markers" are expressed in any and/or all benign disorders and cancers.

However, the scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art. The instant specification is not enabling for claims drawn to providing a means for discriminating between any and/or all benign disorders and cancers by calculating a ratio based on at least two of the measured concentrations of either IGF-I, IGFBP-3, and PSA. The specification (page 12, paragraph 0041) teaches that permutations of IGF-I/free

PSA, intact IGFBP-3/free PSA, (IGF-I/total IGFBP-3)/free PSA, (intact IGFBP-3/total IGFBP-3)/PSA, and (IGF-I + intact IGFBP-3)/free PSA and measurement of intact IGFBP-3 alone have been shown to be useful indicators of prostate cancer. The specification (page 30, paragraph 0072) further discloses the identification of significantly higher levels of IGF-I and intact IGFBP-3 in those patients with CaP (*prostate cancer*) than those with BPH (*benign prostate hyperplasia*). Specifically, the specification (page 30, paragraph 0072 to page 31) teaches that the IGF-I/free PSA and intact IGFBP-3/free PSA ratios demonstrates potential for significant CaP diagnostic improvements.

The instant specification provides insufficient guidance and objective evidence to predictably enable one of skill in the art to use the invention as broadly claimed without resorting to undue experimentation. Those of skill in the art would recognize the unpredictability of discriminating between any and/or all benign disorders and cancers by calculating a ratio based on at least two of the measured concentrations of IGF-I, IGFBP-3, and PSA. For example, one of ordinary skill in the art would recognize the unpredictability of using PSA as a diagnostic for any and/or all benign disorders and cancers such as breast cancer. Malleno *et al.* (Breast Cancer Res. 2001, 3:238-243) addresses whether or not prostate specific antigen (PSA/hK3) is a future player in the filed of breast cancer diagnostics. Specifically, Malleno *et al.* (abstract) teach that although several studies have suggested new biological functions for PSA in breast physiology, more studies are needed to enlist PSA unequivocally as an additional weapon in the anticancer armory in breast cancer diagnostics. For instance, Black *et al.* (Breast Cancer Res. 2000, 59:1-14) asserts that PSA is produced by the majority of breast tumors and is a favorable indicator of prognosis in breast cancer (abstract). In contrast, other studies have suggested that induction of serum PSA is also associated with an "unfavorable" prognosis in breast cancer patients with tumors. For example, Romppanen *et al.* (Br. J. Cancer 1999, 79 (9/10), 1583-1587) evaluated the measurement of serum prostate specific antigen (PSA) as a potential diagnostic test for differentiation between women with breast cancer and those with benign breast disease (abstract). Romppanen *et al.* concluded that serum total PSA cannot be used to distinguish between healthy woman and/or women with breast cancer or benign breast cancer (abstract). In addition, Hely *et al.* (Anticancer Res. 1999, 19: 2563-2565) studied the correlation between PSA immunoreactivity of tissues from one hundred women with malignant breast tumors with tumor tagging, histomorphological tumor type and biochemical estrogen and progesterone receptor content. In this study, Hely *et al.* found no significant correlation between

PSA and other prognostic markers which indicates that PSA detection by immunohistochemistry seems not to be helpful in prognostic evaluation of breast cancer (abstract). Thus, in order to practice the claimed invention, the skilled artisan would not have found sufficient guidance in the specification for discriminating between any and/or all benign disorders and cancers by calculating a ratio based on at least two of the measured concentrations of either IGF-I, IGFBP-3, and PSA.

In view of the teachings above, and the lack of guidance and or exemplification in the specification, it would not be predictable that the method would function as contemplated. Thus, it would require undue experimentation by one of skill in the art to practice the invention as claimed.

Claim Rejections - 35 USC § 102

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 25-30 and 40 are rejected under 35 U.S.C. 102(e) as being anticipated by Pollak *et al.* (U.S. 6,645,770, 1998).

In the instant case, the claims are drawn to a diagnostic method comprising: (i) collecting a body fluid from an individual; (ii) measuring an insulin-like growth factor binding protein (IGFBP) concentration; (iii) measuring a growth factor concentration; (iv) measuring a tumor marker concentration; and (v) calculating an indicator ratio based upon at least two of the measured concentration, wherein the indicator ratio provides a means for discriminating between benign disorders and cancer. The claims are further drawn to wherein the growth factor is IGF-I (claim 26), the IGFBP is IGFBP-3 either total or intact (claim 27-28), and the tumor marker is PSA (claim 28). Moreover, the claims are further drawn to wherein the benign disorder is benign prostate disorder and the cancer is prostate (claim 40).

Pollack *et al.* disclose (column 1, lines 25-32) methods of assessing the risk of developing prostate cancer in an individual involving measuring IGF-I and/or insulin-like growth factor binding protein-3 (IGFBP-3) in a specimen, wherein high levels of IGF and/or low levels of IGFBP correlate with increased risk of developing prostate cancer. Furthermore, the patent (column 1, lines

33-38) provides a method involving determining the IGF/PSA status of an individual wherein the determination of IGF status is combined with a measurement of prostate specific antigen (PSA) levels. In addition to predicting prostate cancer, Pollack *et al.* (column 5, lines8-17) teach that the method can also be useful in differentiating cancer from other prostatic diseases, including, but limited to benign prostatic hyperplasia. Lastly, with regards to the IGFBP-3, the patent (column 5, lines 51-53) teaches that total, complexed and/or free IGFBP-3 may be measured.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 25-30 and 40 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2 and 4 of U.S. Patent No. 6,448,086.

Although the conflicting claims are not identical, they are not patentably distinct from each other because a species anticipates a genus. In the instant case, a method of discriminating between benign prostate disorders and prostate cancer by calculating a indicator ratio of either intact IGFBP-3/free PSA or IGF-I/free PSA claimed in the conflicting patent appears to fall within the same scope of the genus discriminating between benign disorders and cancer by calculating an indicator ratio based on at least two measured concentrations of either IGF-I, IGFBP-3 or PSA claimed in the application being examined and, therefore, a patent to discriminating between benign disorders by calculating an indicator ratio based on at least two measured concentrations of either IGF-I, IGFBP-3 or PSA would necessarily, extend the rights of discriminating between benign prostate

disorders and prostate cancer by calculating a indicator ratio of either intact IGFBP-3/free PSA or IGF-I/free PSA should the application being examined issue as a patent after the conflicting patent.

Therefore, NO claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
1/10/05